PATENT COOPERATION TREATY

From the:
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

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MADDERNS
15 OCT 2003

PCT

WRITTEN OPINION
(PCT Rule 66)

Date of mailing *(day/month/year)* 10 OCT 2003

Applicant's or agent's file reference
12232PCT CMH:SJ

REPLY DUE within **TWO MONTHS** from the above date of mailing

International Application No.	International Filing Date *(day/month/year)*	Priority Date *(day/month/year)*
PCT/AU03/00410	4 April 2003	4 April 2002

International Patent Classification (IPC) or both national classification and IPC
Int. Cl. [7] A61K 7/16, 31/155, 31/428, 31/7028, 33/30

Applicant
H A MILTON HOLDINGS PTY LTD et al

1. This written opinion is the **first** drawn by this International Preliminary Examining Authority.
2. This opinion contains indications relating to the following items:.

I	[X]	Basis of the opinion
II	[ ]	Priority
III	[ ]	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	[ ]	Lack of unity of invention
V	[X]	Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	[ ]	Certain documents cited
VII	[ ]	Certain defects in the international application
VIII	[X]	Certain observations on the international application

3. The **FINAL DATE** by which the international preliminary examination report must be established according to Rule 69.2 is:
4 August 2004

4. The applicant is hereby **invited to reply** to this opinion.

When? See the **Reply Due** date indicated above. However, the Australian Patent Office will not establish the Report before the earlier of (i) a response being filed, or (ii) one month before the **Final Date** by which the international preliminary examination report must be established. The Report will take into account any response (including amendments) filed before the Report is established.
If no response is filed by 1 month before the Final Date, the international preliminary examination report will be established on the basis of this opinion.
Applicants wishing to have the benefit of a further opinion (if needed) before the report is established should ensure that a response is filed at least **3 months before the Final Date** by which the international preliminary examination report must be established.

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3.
For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4*bis*.
For an informal communication with the examiner, see Rule 66.6.

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WRITTEN OPINION

International application No.
PCT/AU03/00410

I. Basis of the opinion

1. With regard to the elements of the international application:*

[X] the international application as originally filed.

[ ] the description, pages , as originally filed,
pages , filed with the demand,
pages , received on with the letter of

[ ] the claims, pages , as originally filed,
pages , as amended under Article 19,
pages , filed with the demand,
pages , received on with the letter of

[ ] the drawings, pages , as originally filed,
pages , filed with the demand,
pages , received on with the letter of

[ ] the sequence listing part of the description:
pages , as originally filed
pages , filed with the demand
pages , received on with the letter of

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language which is:

[ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

[ ] the language of publication of the international application (under Rule 48.3(b)).

[ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the written opinion was drawn on the basis of the sequence listing:

[ ] contained in the international application in printed form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form.

[ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. [ ] The amendments have resulted in the cancellation of:

[ ] the description, pages

[ ] the claims, Nos.

[ ] the drawings, sheets/fig.

5. [ ] This opinion has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed"*

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-24	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	1-24	NO
Industrial applicability (IA)	Claims	1-24	YES
	Claims		NO

2. Citations and explanations

Citations

The opinion has considered the following documents cited in the International Search Report:

D1: EP 0026252 A

D2: WO 01/22930 A

D3: EP 0181161 A

D4: Neohesperidine Dihydrochalcone (NHDC). Product Information

D5: EP 0920857 A

D1 discloses an oral formulation comprising chlorhexidine gluconate, sodium saccharine, zinc acetate, fruit essence and other conventional components of oral formulations, see example 7.

D2 discloses an oral formulation comprising chlorhexidine gluconate, sodium saccharin, zinc acetate, sorbitol and other conventional components of oral formulations, see page 9 table.

D3 discloses an oral formulation comprising chlorhexidine gluconate, sodium saccharin, zinc gluconate, flavour mix (mint/spearmint) and other conventional components of oral formulations, see example 1-2.

D4 discloses the synergistic sweetening effect Neohesperidine Dihydrochalcone (NHDC) has with other sweeteners such as saccharin. This document further discloses the use of NHDC in tooth pastes and mouth-wash.

D5 discloses an oral formulation comprising chlorhexidine gluconate, saccharin, zinc gluconate, xylitol and other conventional components of oral formulations, see page 4 table A.

Novelty and Inventive Step

The invention defined in claim 1-24 encompass oral formulations comprising chlorhexidine, a zinc salt, a masking/flavouring component comprising an immediate action sweetening agent, and a sweetening agent having a delayed but prolonged effect, and other conventional components of oral formulations.

Continued in Supplementary Box I

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The invention defined in claims 1-3, 6-24 are not fully supported by the description. There is only support for the sweetening agent having a delayed but prolonged effect to be Neohesperidine Dihydrochalcone (NHDC). The inventive concept appears to be that NHDC is able to mask the taste of chlorhexidine in oral formulations, however as currently drafted the claims are not restricted to this feature. For this reason the invention defined in claims 1-24 is not fully supported by the description.

Supplemental Box I
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of V

Novelty and Inventive Step (continued..)

The invention defined in claims 1-24 are novel in light of D1-D5. D4 discloses the synergistic sweetening effect of NHDC and therefore does not disclose the claimed invention. Even though D1-D3, D5 disclose compositions comprising chlorhexidine, a zinc salt, a masking/flavouring component comprising an immediate action sweetening agent (such as saccharin or xylitol), and other conventional components of oral formulations, none of these documents include the use of a **sweetening agent having a delayed but prolonged effect, such as NHDC,** in addition to conventional sweetening agents. In light of this there is no disclosure or suggestion in the prior art of an oral formulation comprising chlorhexidine, a zinc salt, a masking/flavouring component comprising an immediate action sweetening agent, **and a sweetening agent having a delayed but prolonged effect**, and other conventional components of oral formulations. Therefore claims 1-24 are novel in light of D1-D4

However the invention defined in claims 1-24 do not involve an inventive step when D1-D3, D5 is read in the light of D4. D1-D3, D5 disclose oral compositions comprising chlorhexidine and conventional sweetener but without a sweetening agent having a delayed but prolonged effect, such as NHDC. D4 discloses the synergistic sweetening effect NHDC has with other sweeteners such as saccharin and that NHDC can be used in tooth pastes and mouth-wash. This document further discloses the NHDC has a delay before producing a sweetening effect. The problem in the current application is that current oral formulations comprising chlorhexidine and conventional sweeteners have an unpleasant taste due to this compound, see page 6 paragraph 3 of the instant application. In light of this and upon reading D1-D3, D5 in light of D4 a person skilled in the art would be directly led to include NHDC in oral formulation comprising chlorhexidine and conventional sweetening agents to improve the taste of the oral formulation. For this reason the invention defined in claims 1-24 do not involve an inventive step.

Industrial Applicability

Claims 1-24 are industrial applicable.

stirring. Allow to thicken.

EXAMPLE 2: Toothpaste Formulation

The formulation is similar to that of Example 1, except that 0.01-0.22% w/w of sodium fluoride is added to the aqueous phase B.

EXAMPLE 3: Clinical Studies

Introduction

A study was carried out in the Department of Dentistry, University of Adelaide, in conjunction with Hamilton Laboratories, to test the effect of a new formulation of a toothpaste containing chlorhexidine (CHX) gluconate (as per Example 1) on dental plaque formation. Slurries of the toothpastes being tested were prepared and used as rinses, with subjects abstaining from mechanical plaque control for 4 days. The slurry method is used because mechanical plaque control alone, performed by a skilled person, would reduce dental plaque formation, with or without the use of a toothpaste or antibacterial agent. A commercial Oral Rinse (mouthwash) formulation from Zila Inc (Peridex, containing 0.12% w/w chlorhexidine gluconate solution) was chosen as a positive control because of its well documented ability to suppress plaque formation.

Methods

Subjects

Volunteers participating in the study were non-smokers, in good general health and included both women and men between 20 and 55 years of age. They did not use any